

IN THE SPECIFICATION:

- Please replace the paragraphs that extend from page 16, line 3, to page 18, line 19, with the following:

Fig. 1 is a scanning electron micrograph (SEM) of an article of the invention showing the voids of a scaffold and the interconnecting pores between the voids;

Fig. 2 is a SEM image of Polyether polyurethane biomaterial placed in a chamber with a 0.45 μ m filter, implanted subcutaneously in the rat animal model and explanted after 8 weeks. Note the integrity of the voids of the biomaterial. The structure of the voids is similar to that for the control sample (Fig. 3) demonstrating no evidence of Environmental Stress Cracking (ESC);

Fig. 3 is a SEM image of Polyether polyurethane biomaterial control sample which was not implanted in the rat model;

Fig. 4 is a SEM image of Polyether polyurethane biomaterial placed in a chamber with a 0.45 μ m filter, implanted subcutaneously in the rat animal model and explanted after 8 weeks. As in Fig. 2, note the integrity of the voids of the biomaterial. The structure of the voids is similar to that for the control sample (Fig. 3) demonstrating no evidence of ESC;

Fig. [[1.4]] 5 is a SEM image (at high magnification) of Polyether polyurethane biomaterial placed in a chamber with a 0.45µm filter, implanted subcutaneously in the rat animal model and explanted after 8 weeks. Note the integrity of the void of the biomaterial. The structure of the voids is similar to that for the control sample (Fig. [[1.2]] 3) demonstrating no evidence of ESC;

Fig. [[1.5]] 6 is a SEM image of Polyether polyurethane biomaterial placed in a chamber with a 3.0µm filter, implanted subcutaneously in the rat animal model and explanted after 26 weeks. Note the integrity of the voids of the biomaterial and the cellular deposition on the biomaterial. There is no evidence in this SEM image of ESC;

Fig. [[2.1]] 7 is a photomicrograph of the scaffold of Example 1 stained with Haemoxilin and Eosin (H&E), 12 weeks following implantation. Note the presence of numerous macrophage cells throughout the scaffold and the presence of blood capillaries (indicated by the arrow) in the centre of the scaffold;

Fig. [[2.2]] 8 represents images from 2 rat explants at 26 weeks, which were stained positive with rat monoclonal antibodies to ED₁ cells (immature macrophage and monocytes);

Fig. [[2.3]] 9 is a photomicrograph (3.2X) of the scaffold of Example 1, explanted at 12 weeks and stained with H&E. Note the absence of a fibrotic layer between the scaffold and the muscle;

Fig. [[2.4]] 10 is a photomicrograph (3.2X) of an intramuscular implant of Example 1, explanted at 26 weeks and stained with H&E. Note the presence of translucent fat cells to the left of the implant;

~~Fig. 2.5 represents~~ Figs. 11(a) and 11(b) represent images from a rat explant at 26 weeks, which stained negative with CD⁴ and CD⁸ rat monoclonal antibodies. There was no evidence of CD⁴ or CD⁸ lymphocytes throughout the scaffold;

Fig. [[2.6]] 12 is a photomicrograph (10X) of the scaffold at 8 weeks after venous implantation. Numerous inflammatory cells (macrophage) are evident throughout the scaffold. Also note there is no fibrotic wall between the scaffold and the venous wall;

Fig. [[2.7]] 13 illustrates the expression of α -smooth muscle actin throughout the scaffold 8 weeks post implantation. The α -smooth muscle actin is present in the walls of the capillaries forming the capillary bed;

Fig. [[2.8]] 14 is a photomicrograph (50X) of the scaffold 8 weeks after venous implantation. Note the blood capillary in the top left of the photomicrograph with red blood cells present in the lumen of the capillary. The flattened elongated cells defining the capillary wall are characteristic of the morphology of endothelial cells;

Fig. [[2.9a]] 15 is a photomicrograph of collagen deposition stained blue by MSB one week following implantation of the scaffold of Example 1;

Fig. [[2.9b]] 16 is a 40X magnification of a photomicrograph of collagen deposition stained blue by MSB 4 weeks following implantation of the scaffold of Example 1; and

Fig. [[3.1]] 17 is a photomicrograph of a polycarbonate polyurethane material of the invention.

- Page 19, lines 1-3, please replace the paragraph with the following:

A Scanning Electron Microscopy (SEM) image of an article of this invention is provided in Figure [[A]] 1. This image illustrates the voids of the scaffold and the interconnecting pores between the voids.

- Please replace the paragraphs that extend from page 32, line 25, to page 34, line 19, with the following:

Samples of this biomaterial were placed in sealed acrylic chambers and implanted in the subcutaneous cavities of rats. The samples were explanted at a number of time points up to 6 months post implantation. The biomaterial samples were examined by Scanning Electron Microscopy (SEM). No evidence of degradation was

observed in any of the explanted samples as demonstrated in ~~Figures 1.1 to 1.5~~ Figures 2-6.

In vivo response

Evidence of these features of this tissue engineering scaffold is provided in photographs of the appropriate sections in ~~Figure 2.1 to 2.9~~ Figures 7-16.

This scaffold was also implanted in the gluteal muscle of rats and left for up to 6 months. The histological analysis conducted on the explants indicated that;

- ◆ The biomaterial scaffold stimulated a macrophage response (Figure ~~[[2.1]] 7~~). The macrophage response was atypical in that a significant presence of immature macrophage cells (ED1 cells) was observed. (Figure ~~[[2.2]] 8~~)
- ◆ Angiogenesis was clearly observed within the bulk of the scaffold. This means that cells growing within the material have constant access to nutrients etc. transported through the new vascular network. (Figure ~~[[2.1]] 7~~)
- ◆ The absence of a fibrotic layer surrounding the implant is a unique observation for this type of scaffold. A fibrotic layer surrounding the implant was not observed at any time point. (Figure ~~[[2.3]] 9~~)
- ◆ Quantities of fat cells were observed lying in the spaces surrounding the implant and has hither to fore not been observed in a tissue scaffold. This indicates the degree to which the material was tolerated. (Figure ~~[[2.4]] 10~~)

- ◆ The absence of a T-lymphocyte response was evidenced by immunohistochemical staining indicating the absence of CD4 and CD8 antibodies. This result is also significant in that there is no painful inflammatory response induced as a result of the implantation. (~~Figure 2.5~~ Figures 11(a) and 11(b))

The biomaterial scaffold was implanted in the vasculature of a rabbit for a period of up to 3 months. The results of the study demonstrated that ;

- ◆ There was evidence of numerous cell populations within the biomaterial was observed when the material was implanted in the vasculature of a rabbit and the excised specimens were examined histologically. The results of the study indicated that;
- ◆ The material induced a macrophage response. (Figure ~~[[2.6]]~~ 12)
- ◆ The scaffold stained positive for the α -actin filaments of smooth muscle cells (Figure ~~[[2.7]]~~ 13) and endothelial cell. These cells were organised in the form of blood capillaries which formed a vascular bed throughout the scaffold. (Figure ~~[[2.8]]~~ 14)
- ◆ There was no fibrotic layer surrounding the implant, indicating that the scaffold was very well tolerated in this in vivo model. (Figure ~~[[2.6]]~~ 12)
- ◆ A number of different cell types co-existed within the biomaterial including fibroblasts, smooth muscle cells, endothelial cells and white blood cells. (Figures ~~2.6, 2.7 and 2.8~~ 12-14)
- ◆ Fibroblast cells within the material secreted a number of different types of collagen. This demonstrates that the cells within the material are secreting proteins of the correct phenotype. (~~Figure 2.9a and 2.9b~~ Figures 15 and 16)

- Page 36, lines 9-12, please replace the paragraph with the following:

This biomaterial was directly implanted directly in the gluteal muscle of rats and left for up to 2 weeks. The histological analysis conducted on the explants indicated that the inflammatory response was comparable to the inflammatory response obtained with the material of example A. (Figure [[15]] 6).

- Page 55, lines 20-28, please replace the paragraphs with the following:

The chemistry and process for some preferred polyether and polycarbonate polyurethanes which may be used in the invention are described in more detail in our co-pending PCT application No. _____ PCT/IE00/00056 filed May 8, 2000, the entire contents of which are herein incorporated by reference (SALV12).

Solvent extraction techniques which are preferably used in the invention are described in more detail in our co-pending PCT application No. _____ PCT/IE00/00058 filed May 8, 2000, the entire contents of which are herein incorporated by reference (SALV14).